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(54) Title: TRUNCATED FRAGMENTS OF ALPHA-SYNUCLEIN IN LEWY BODY DISEASE

(57) Abstract: The application identifies novel fragments of alpha-synuclein in patients with Lewy Body Disease (LBD) and transgenic animal models thereof. These diseases are characterized by aggregations of alpha-synuclein. The fragments have a truncated C-terminus relative to full-length alpha-synuclein. Some fragments are characterized by a molecular weight of about 12 kDa as determined by SDS gel electrophoresis in tricine buffer and a truncation of at least ten contiguous amino acids from the C-terminus of natural alpha-synuclein. The site of cleavage preferably occurs after residue 117 and before residue 126 of natural alpha-synuclein. The identification of these novel fragments of alpha-synuclein has a number of application in for example, drug discovery, diagnostics, therapeutics, and transgenic animals.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/37875

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A61K 49/00(2006.01);A01N 61/00(2006.01),37/18(2006.01);A61K 31/00(2006.01),38/00(2006.01);G01N 33/00(2006.01);A01K 67/00(2006.01),67/033(2006.01)

USPC: 424/9.1;514/1,2;800/3,9,12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/9.1; 514/1,2; 800/3,9,12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | TSIM, K.W. et al., Monoclonal antibodies specific for the different subunits of asymmetric acetylcholinesterase from chick muscle. J. Neurochem. July 1988, Vol. 51, No. 1, pages 95-104, see abstract | 52 |
| X | HAMBURGER, A.W., et al., Isolation and characterization of monoclonal antibodies reactive with endothelial cells. Tissue Cell. 1985, Vol. 17. No. 4, pages 451-459, abstract | 52 |
| X | US 6,780,971 B2 (Wolozin et al) 24 August 2004 (24.08.2004), column 17, lines 53-62 | 1, 4 |
| A | TAKAHASHI, M. Phosphorylation of alpha-synuclein characteristic of synucleinopathy lesions is recapitulated in alpha-synuclein transgenic Drosophila. Neuroscience Letters. 2003, Vol. 336, pages 155-158. | 1-52 |



Further documents are listed in the continuation of Box C.



See patent family annex.

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PCT/US05/37875**C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | OKOCHI, M. Constitutive Phosphorylation of the Parkinson's Disease Associated alpha-Synuclein. <i>The Journal of Biological Chemistry</i> . January 2000, Vol 275. No. 1, pages 390-397. | 1-52 |
| A | KIM, T.D. et al. Structural Changes in alpha-Synuclein Affect its Chaperone-like Activity In Vitro. <i>Protein Science</i> . 2000, Vol 9. pages 2489-2496 | 1-52 |
| A | HOYER, W. et al., Dependence of alpha-Synuclein Aggregate Morphology on Solution Conditions. <i>J. Mol. Biol.</i> 2002, Vol 322, pages 383-393. | 1-52 |

INTERNATIONAL SEARCH REPORT

International application No.
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Continuation of B. FIELDS SEARCHED Item 3:
Google, EAST, STN
search terms: alpha-synuclein, phosphorylated, 1-115, 1-133, 1-135, 12C6, 7G8